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Applicant: Gabriele MULTHOFF
Application No. 09/646,835
Attorney Docket No. 105032.991230
(former ref. no. 40740)

IN THE CLAIMS:

Claims 1-30 (Canceled)

Claim 31 (Currently Amended) A method for the ex vivo ~~ex~~-activation of NK-cells, comprising: contacting NK cells in a physiological suspension with an isolated Hsp70 protein of SEQ ID NO: 1 or an isolated ~~an~~ isolated C-terminal fragment of Hsp70, wherein said fragment is selected from the group consisting of amino acids 384-641 of SEQ ID NO: 1, derivatives thereof, an isolated polypeptide having 70% or greater homology to amino acids 384-641 of SEQ ID NO: 1 and derivatives thereof, wherein said isolated protein, fragment, polypeptide and derivatives thereof induce an under conditions which comprise stimulation of immune response by NK cells, and further said response increases cytolytic activity of the NK cells or stimulates proliferation of the NK cells.

 Claim 32 (Original) The method of claim 31, wherein said activation of said cells further comprises stimulation of proliferation and/or an increase in cytotoxicity.

Claim 33 (Original) The method of claim 31, wherein said physiological suspension containing NK cells comprises a peripheral mononuclear blood cell fraction or fractions thereof.

Claim 34 (Original) The method of claim 31, wherein said suspension further comprises cells expressing cell-surface Hsp70.

Claim 35 (Original) the method of claim 34, wherein said expressing cells comprise diseased cells from a patient.

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Claim 36 (Original) The method of claim 35, wherein said diseased cells are selected from the group consisting of leukemia cells, lymphoma cells, tumor cells, metastasizing cells of solid tumors, and cells from a virally, mycotically and/or bacterially infected patient.

Claim 37 (Currently Amended) The method of any one of claims 31-36, wherein said contacting is carried out for at least 3 hours.

Claim 38 (Original) The method of claim 37, wherein said contacting is carried out for 4 days.

Claim 39 (Original) The method of claim 37, wherein said conditions further comprise addition of a cytokine.

Claim 40 (Original) The method of claim 39, wherein the cytokine is an interleukin.

Claim 41 (Original) The method of claim 40, wherein said interleukin is selected from the group consisting of IL-2, IL-12, and IL-15.

Claim 42 (Original) A method for the in vivo activation of the immune system in a patient in need thereof comprising:

- i) administering to said patient a pharmaceutically effective amount of NK cells obtained by the method of claim 37 and
- ii) optionally administering to said patient, concurrently or subsequently, a pharmaceutically effective amount of a Hsp70 protein of SEQ ID


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NO: 1 or a C-terminal fragment of Hsp70, wherein said fragment is selected from the group consisting of amino acids 384-641 of SEQ ID NO: 1, derivatives thereof, a polypeptide having 70% or greater homology to amino acids 384-641 of SEQ ID NO: 1 and derivatives thereof.

Claim 43 (Original) The method of claim 42, where said patient is suffering from a disease selected from the group consisting of cancerous, infectious and autoimmune diseases.

Claim 44 (Canceled)

Claim 45 (Currently Amended) The method of claim 44-42, wherein said administration further comprises addition of a cytokine.

 Claim 46 (Original) The method of claim 45, wherein said cytokine is an interleukin.

Claim 47 (Original) The method of claim 46, wherein said interleukin is selected from the group consisting of IL-2, IL-12, and IL-15.

Claim 48 (Original) The method of claim 43, wherein said cancerous diseases are selected from the group consisting of tumors, solid tumors, metastatic tumors, leukemias and lymphomas.

Claim 49 (Original) The method of claim 43, wherein said infectious diseases are viral, mycotic or bacterial diseases.

Claim 50 (Original) A pharmaceutical composition comprising a Hsp70


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protein of SEQ ID NO: 1 or a C-terminal fragment of Hsp70, wherein said fragment is selected from the group consisting of amino acids 384-641 of SEQ ID NO: 1, derivatives thereof, a polypeptide having 70% or greater homology to amino acids 384-641 of SEQ ID NO: 1 and derivatives thereof, and a pharmaceutically acceptable carrier, excipient or diluent.

Claim 51 (Original) The composition of claim 50, wherein said protein or fragment is present at a concentration of about 10 µg/ml to about 1000 µg/ml.

Claim 52 (Original) The composition of claim 50, wherein said protein or fragment is of human origin.

Claim 53 (Original) The composition of claim 50, wherein said protein or fragment is recombinant.

 Claim 54 (Original) A pharmaceutical composition comprising NK cells activated by the method of claim 31.

Claim 55 (Original) A method for in vivo activation of the immune system in a patient in need thereof comprising administering to said patient a pharmaceutically effective amount of a Hsp70 protein of SEQ ID NO: 1 or a C-terminal fragment of Hsp70, wherein said fragment is selected from the group consisting of amino acids 384-641 of SEQ ID NO: 1, derivatives thereof, a polypeptide having 70% or greater homology to amino acids 384-641 of SEQ ID NO: 1 and derivatives thereof.


Claim 56 (Original) The method of claim 55, where said patient is suffering from a disease selected from the group consisting of cancerous, infectious and

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autoimmune disease

Claim 57 (Canceled)

Claim 58 (Currently Amended) The method of claim ~~56~~ 55, wherein
said administration further comprises addition of a cytokine.

 Claim 59 (Original) The method of claim 58, wherein said cytokine is an
Interleukin.

Claim 60 (Original) The method of claim 59, wherein said interleukin is
selected from the group consisting of IL-2, IL-12 and IL-15.
